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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/809,425

03/26/2004

Mai Levite

LEVITE3

8418

1444 7590 10/08/2008
BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER

JUEDES, AMY E

ART UNIT

PAPER NUMBER

1644

MAIL DATE

DELIVERY MODE

10/08/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/809,425	Applicant(s) LEVITE, MAI	
	Examiner AMY E. JUEDES	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 6/30/08.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-27 is/are pending in the application.
- 4a) Of the above claim(s) 20-22 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-19, 23, 24, 26 and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's election of group I, drawn to a method for upregulating T-cell activity in a mammalian subject employing glutamate or a glutamate analog, claims 17-19 and 23-27, in the reply filed on 6/30/08, is acknowledged. Applicant has further elected neoplastic disease as the species of subject to be treated. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 20-22 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claim 25 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species.

Claims 17-19, 23-24, and 26-27 read on the elected invention and are being acted upon.

2. In view of Applicant's cancellation of previously pending claims 1-16, all of the previous grounds of rejection are withdrawn. However, Applicant's arguments relevant to the new grounds of rejection will be addressed below.

3. The following are new grounds of rejection necessitated by Applicant's amendment to the claims.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 26 is rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed,

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specifically:

A method for upregulating T cell activity comprising treating a T cell population with a molecule that stimulates an "ionotropic" glutamate receptor.

Applicant indicates that support for the new limitations of Claim 1 can be found at page 33 of the specification.

A review of the specification fails to reveal support for the new limitations.

The specification on page 28 discloses that the invention employs GluR3 glutamate receptor regulation. However, GluR3 receptor regulation has a narrower scope than "ionotropic" glutamate receptor. At page 33 the specification further discloses that upregulating glutamate analogs may be an ionotropic upregulator. However, the instant claims encompass a method comprising treating T cells with a molecule (including an antibody or a polynucleotide) that stimulates an ionotropic glutamate receptor. The disclosure of a glutamate analog that stimulates said ionotropic receptor has a narrower scope than the instant claims which encompass antibodies and polynucleotides that stimulate said receptor.

6. Claims 17, 19, 23-24, and 26-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is insufficient written description to demonstrate that applicant was in possession of the claimed genus of glutamate "analogs".

The instant claims are drawn to a method employing a glutamate "analog" that has a substantial degree of structural identity to glutamate and that stimulates glutamate receptor activation, as measured by upregulation of T-cell cytokine secretion, adhesion, or chemotactic migration. Glutamate receptor exists as a myriad of different subtypes (for example there are three types of ionotropic receptors, and at least 8 different metabotropic glutamate receptors). Furthermore, it is noted that a "substantial" identity is completely relative, and the specification does not provide any guidance as to what

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structural features are required (for example, the specification does not disclose a required core chemical structure or examples of functional groups that might be altered). Therefore, the specification does not provide a correlation between the structure of the glutamate "analogs" and the function of stimulating any glutamate receptor. The specification on page 33 discloses 5 glutamate analogs. However, it is not even clear that the disclosed analogs are those that share a "substantial" degree of structural similarity to glutamate, as recited in the instant claims. For example, both AMPA and quisqualic acid are heterocyclic compounds, while glutamate does not have a ring structure. Additionally, the 5 compounds are not representative of the broad range of analogs encompassed by the claims, which act as agonists for any glutamate receptor, including the 8 metabotropic receptors as well as the numerous ionotropic types of receptors. Additionally, even when the claims are limited to analogs that stimulate the GluR3 receptor, the specification only discloses a single species of said analog, AMPA. A single species is not sufficiently representative of the broad genus of GluR3 analogs encompassed by the claims. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

7. Claims 17-19, 23-24, and 26-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for upregulating T cell cytokine secretion, T cell adhesion, or T cell chemokine mediated migration by stimulating glutamate receptor activation,
does not reasonably provide enablement for:

a method for upregulating T cell activity by stimulating glutamate receptor activation.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir.

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1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The instant claims are drawn to a method of upregulating T cell activity comprising exposing T cells to glutamate or a glutamate analog. This encompasses upregulating a wide range of activities of different types of T cells (for example activities of regulatory T cells, CD4 T cells, CD8 T cells, including activities such as proliferation, cytokine production, etc.). It is known that T cells express receptors for glutamate, and that exposure of T cells to glutamate can increase calcium release (see Lombardi et al.). However, despite increasing calcium release, glutamate decreases T cell proliferation (see Lombardi et al., Fig. 7). Thus, while glutamate might be capable of upregulating certain T cell activities, for example calcium release, the prior art teaches that glutamate does not increase all T cell activities (for example T cell proliferation), as is encompassed by the instant claims.

Thus, based on the state of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims. The instant specification demonstrates that T helper cell clones treated with glutamate display increased production of cytokines and that peripheral blood T cells treated with glutamate display increased chemotaxis. However, this is not commensurate in

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scope with the instant claims, which encompass increasing any activity of any type of T cell, not just cytokine production by T helper cells or chemotaxis of peripheral blood T cells. Thus, given the state of the art and the lack of guidance provided by the instant specification, the method as broadly claimed must be considered highly unpredictable. Given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

Applicant's arguments filed 1/24/08 have been fully considered, but they are not persuasive.

Applicant argues that as long as one T cell activity is upregulated the terms of the claims are met, and those of ordinary skill in the art reading the present specification would be able to stimulate glutamate receptor activation and obtain the T cell activity upregulation described in the specification.

The fact that the specification teaches how to upregulate certain T cell activities is not sufficient. The specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. See MPEP 2164.08.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-18, 23-24, and 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Winter et al., 1999, as evidenced by Droge et al. 1988 (of record).

Winter et al. teach a method of enhancing the anti-tumor T cell response (i.e. a method of upregulating a "T cell activity") comprising administering T cells to a subject with a tumor (see page 4465 in particular). Winter et al. further teach that the T cells are cultured ex-vivo in RPMI medium before administration (see page 4463 in particular). As evidenced by Droge et al., RPMI medium contains glutamate (see pages 126-127). Thus, Winter et al. have inherently treated the T cells ex-vivo with glutamate, as recited in the instant

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claims. Said glutamate treatment would inherently stimulate the glutamate receptor, including the GluR3 receptor.

Thus, the reference clearly anticipates the invention.

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 6am - 2pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amy E. Juedes, Ph.D.
Patent Examiner
Technology Center 1600

/G.R. Ewoldt/
Primary Examiner, Art Unit 1644